TOXICOLOGICAL PROFILE FOR STRONTIUM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

July 2001

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

UPDATE STATEMENT

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry Division of Toxicology/Toxicology Information Branch 1600 Clifton Road NE, E-29 Atlanta, Georgia 30333

FOREWORD

This toxicological profile is prepared in accordance with guidelines developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;
- (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and
- (C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public. We plan to revise these documents in response to public comments and as additional data become available. Therefore, we encourage comments that will make the toxicological profile series of the greatest use.

Comments should be sent to:

Agency for Toxic Substances and Disease Registry Division of Toxicology 1600 Clifton Road, N.E. Mail Stop E-29 Atlanta, Georgia 30333

Background Information

The toxicological profiles are developed by ATSDR pursuant to Section 104(i) (3) and (5) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund) for hazardous substances found at Department of Energy (DOE) waste sites. CERCLA directs ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL) and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. ATSDR and DOE entered into a Memorandum of Understanding on November 4, 1992 which provided that ATSDR would prepare toxicological profiles for hazardous substances based upon ATSDR's or DOE's identification of need. The current ATSDR priority list of hazardous substances at DOE NPL sites was announced in the Federal Register on July 24, 1996 (61 FR 38451).

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and is being made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

Jeffrey P. Koplan, M.D., M.P.H.

Administrator

Agency for Toxic Substances and Disease Registry

STRONTIUM vii

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

- **Chapter 1: Public Health Statement**: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.
- **Chapter 2: Relevance to Public Health**: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.
- **Chapter 3: Health Effects**: Specific health effects of a given hazardous compound are reported by *type of health effect* (death, systemic, immunologic, reproductive), by *route of exposure*, and by *length of exposure* (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.7 How Can (Chemical X) Affect Children?

Section 1.8 How Can Families Reduce the Risk of Exposure to (Chemical X)?

Section 3.7 Children's Susceptibility

Section 6.6 Exposures of Children

Other Sections of Interest:

Section 3.8 Biomarkers of Exposure and Effect

Section 3.11 Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-888-42-ATSDR or (404) 498-0110 **Fax:** (404) 498-0057

E-mail: atsdric@cdc.gov Internet: http://www.atsdr.cdc.gov

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include Reproductive and Developmental Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity; and numerous chemical-specific case studies.

STRONTIUM viii

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—Medical Management Guidelines for Acute Chemical Exposures—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

- The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 Phone: 770-488-7000 FAX: 770-488-7015.
- The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 Phone: 800-35-NIOSH.
- The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 Phone: 919-541-3212.
- Radiation Emergency Assistance Center/Training Site (REAC/TS) provides support to the U.S.

 Department of Energy, the World Health Organization, and the International Atomic Energy Agency in the medical management of radiation accidents. A 24-hour emergency response program at the Oak Ridge Institute for Science and Education (ORISE), REAC/TS trains, consults, or assists in the response to all kinds of radiation accidents. Contact: Oak Ridge Institute for Science and Education, REAC/TS, PO Box 117, MS 39, Oak Ridge, TN 37831-0117

 Phone 865-576-3131 FAX 865-576-9522 24-Hour Emergency Phone 865-576-1005 (ask for REAC/TS) e-mail: cooleyp@orau.gov website (including emergency medical guidance): http://www.orau.gov/reacts/default.htm

Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact:

AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 •
FAX: 202-347-4950 • e-mail: aoec@dgs.dgsys.com • AOEC Clinic Director: http://occ-env-med.mc.duke.edu/oem/aoec.htm.

STRONTIUM ix

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 55 West Seegers Road, Arlington Heights, IL 60005 • Phone: 847-818-1800 • FAX: 847-818-9266.

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHORS(S):

Alfred F. Dorsey, D.V.M Henry G. Abadin, M.S.P.H. Sam Keith, M.S., C.H.P. ATSDR, Division of Toxicology, Atlanta, GA

Margaret E. Fransen, Ph.D.
Gary L. Diamond, Ph.D.
Richard J. Amata, Ph.D.
Syracuse Research Corporation, North Syracuse, NY

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

- 1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.
- 2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.
- 3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

STRONTIUM xii

PEER REVIEW

A peer review panel was assembled for strontium. The panel consisted of the following members:

- 1. Adele L. Boskey, Ph.D., Professor of Biochemistry and Cell and Molecular Biology, Director of Research Hospital for Special Surgery, Weill Medical College of Cornell University, New York, New York,
- 2. Marvin Goldman, Ph.D., Emeritus Professor of Radiation Biology, Department of Surgical and Radiological Sciences, University of California, Davis, California,
- 3. Bruce Muggenburg, D.V.M., Ph.D., Senior Scientist and Veterinary Physiologist, Toxicology Division, Lovelace Respiratory Research Institute, Albuquerque, New Mexico, and
- 4. Robert B. Rucker, Ph.D., Professor of Nutrition and Biological Chemistry, University of California, Davis, California.

These experts collectively have knowledge of strontium's physical and chemical properties, toxico-kinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

STRONTIUM xiv

CONTENTS

FOREWORD .	v
QUICK REFERE	NCE FOR HEALTH CARE PROVIDERS vii
CONTRIBUTOR	S
PEER REVIEW	xiii
LIST OF FIGUR	ES xix
LIST OF TABLE	S
1.1 WHAT 1.2 WHAT 1.3 HOW M 1.4 HOW C 1.5 HOW C 1.6 HOW C 1.7 HOW C 1.8 IS THE TO STR 1.9 WHAT PROTE	LTH STATEMENT
2.1 BACKO UNITED 2.2 SUMM	TO PUBLIC HEALTH
3.1 INTRO	ECTS 33 DUCTION 33 SSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE 35 Inhalation Exposure 37 3.2.1.1 Death 38 3.2.1.2 Systemic Effects 44 3.2.1.3 Immunological and Lymphoreticular Effects 50 3.2.1.4 Neurological Effects 51 3.2.1.5 Reproductive Effects 52 3.2.1.6 Developmental Effects 52 3.2.1.7 Cancer 52 Oral Exposure 54 3.2.2.1 Death 55 3.2.2.2 Systemic Effects 67 3.2.2.3 Immunological and Lymphoreticular Effects 95

		3.2.2.4	Neurological Effects	96
		3.2.2.5	Reproductive Effects	97
		3.2.2.6	Developmental Effects	
		3.2.2.7	Cancer	
	3.2.3		Exposure	
	5.2.5	3.2.3.1	Death	
		3.2.3.2	Systemic Effects	
		3.2.3.3	Immunological and Lymphoreticular Effects	
		3.2.3.4	Neurological Effects	
		3.2.3.4		
			Reproductive Effects	
		3.2.3.6	Developmental Effects	
	2.2.4	3.2.3.7	Cancer	
	3.2.4		Exposure	
		3.2.4.1	Death	
		3.2.4.2	Systemic Effects	
		3.2.4.3	Immunological and Lymphoreticular Effects	
		3.2.4.4	Neurological Effects	
		3.2.4.5	Reproductive Effects	
		3.2.4.6	Developmental Effects	. 112
		3.2.4.7	Cancer	. 112
	3.2.5	Other Ro	outes of Exposure	. 113
		3.2.5.1	Death	
		3.2.5.2	Systemic Effects	
		3.2.5.3	Immunological and Lymphoreticular Effects	
		3.2.5.4	Neurological Effects	
		3.2.5.5	Reproductive Effects	
		3.2.5.6	Developmental Effects	
		3.2.5.7	Cancer	
3.3	CENOT	3.2.3.7 TOXICITY		
3.4			CS	
	3.4.1		on	
		3.4.1.1	Inhalation Exposure	
		3.4.1.2	Oral Exposure	
		3.4.1.3	Dermal Exposure	
	3.4.2		ion	
		3.4.2.1	Inhalation Exposure	. 131
		3.4.2.2	Oral Exposure	. 132
		3.4.2.3	Dermal Exposure	. 136
	3.4.3	Metaboli	sm	. 136
		3.4.3.1	Inhalation Exposure	. 136
		3.4.3.2	Oral Exposure	
		3.4.3.3	Dermal Exposure	
	3.4.4		ion and Excretion	
	5. 1. 1	3.4.4.1	Inhalation Exposure	
		3.4.4.2	Oral Exposure	
		3.4.4.3	Dermal Exposure	
	2 1 5			. 138
	3.4.5		gically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD)	120
	MEGH		OF A CTION	
3.5			OF ACTION	
	3.5.1		okinetic Mechanisms	
	3.5.2	Mechanis	sms of Toxicity	. 157

STRONTIUM xvi

		3.5.3 Animal-to-Human Extrapolations	161
	3.6	ENDOCRINE DISRUPTION	161
	3.7	CHILDREN'S SUSCEPTIBILITY	
	3.8	BIOMARKERS OF EXPOSURE AND EFFECT	168
		3.8.1 Biomarkers Used to Identify or Quantify Exposure to Strontium	169
		3.8.2 Biomarkers Used to Characterize Effects Caused by Strontium	169
	3.9	INTERACTIONS WITH OTHER CHEMICALS	170
	3.10	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	171
	3.11	METHODS FOR REDUCING TOXIC EFFECTS	173
		3.11.1 Reducing Peak Absorption Following Exposure	173
		3.11.2 Reducing Body Burden	
		3.11.3 Interfering with the Mechanism of Action for Toxic Effects	178
	3.12	ADEQUACY OF THE DATABASE	
		3.12.1 Existing Information on Health Effects of Strontium	179
		3.12.2 Identification of Data Needs	182
		3.12.3 Ongoing Studies	193
4.	CHE	MICAL AND PHYSICAL INFORMATION	
	4.1	CHEMICAL IDENTITY	
	4.2	PHYSICAL, CHEMICAL, AND RADIOLOGICAL PROPERTIES	195
5.		DUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	
	5.1	PRODUCTION	
	5.2	IMPORT/EXPORT	
	5.3	USE	
	5.4	DISPOSAL	207
	роті	ENTIAL FOR HUMAN EXPOSURE	211
0.		ENTIAL FOR HUMAN EXPOSURE	
	6.1	OVERVIEW	
	6.2	RELEASES TO THE ENVIRONMENT	
	6.2	VIII VIII VIII VIII VIII VIII VIII VII	
	6.3	ENVIRONMENTAL FATE	
		6.3.1 Transport and Partitioning	222
		VID. 211 1111 1111 1111 1111 1111 1111 111	
	6.4	6.3.2.3 Soils and Sediments	
	0.4		
		6.4.3 Soils and sediments	
	6.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	
	6.6	EXPOSURES OF CHILDREN	
	6.7	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	
	6.8	ADEQUACY OF THE DATABASE	
	0.0	6.8.1 Identification of Data Needs	
		6.8.2 Ongoing Studies.	
		0.0.2 Ongoing budies	230

STRONTIUM xvii

7.	. ANALYTICAL METHODS					
	7.1	BIOLOGICAL MATERIALS	253			
		7.1.1 Internal Strontium Measurements	255			
		7.1.2 <i>In Vivo</i> and <i>In Vitro</i> Radiostrontium Measurements	255			
	7.2	ENVIRONMENTAL SAMPLES				
		7.2.1 Field Measurements of Radiostrontium				
		7.2.2 Laboratory Analysis of Environmental Samples				
	7.3	ADEQUACY OF THE DATABASE	258			
		7.3.1 Identification of Data Needs	258			
		7.3.2 Ongoing Studies	259			
8.	REGU	ULATIONS AND ADVISORIES	261			
9.	REFE	ERENCES	283			
10	. GLC	DSSARY	367			
AF	PPENI	DICES				
	A.	ATSDR MINIMAL RISK LEVELS AND WORKSHEETS	A- 1			
	B.	USER'S GUIDE	B-1			
	C.	ACRONYMS, ABBREVIATIONS, AND SYMBOLS	C-1			
	D.	OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY AND BIOLOGY	D-1			

STRONTIUM xviii

LIST OF FIGURES

3-1.	Levels of Significant Exposure to Strontium—Radiation Toxicity—Inhalation	43
3-2.	Levels of Significant Exposure to Strontium—Chemical Toxicity—Oral	62
3-3.	Levels of Significant Exposure to Strontium—Radiation Toxicity—Oral	76
3-4.	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a	
	Hypothetical Chemical Substance	141
3-5.	Respiratory Tract Compartments in Which Particles May be Deposited	142
3-6.	Reaction of Gases or Vapors at Various Levels of the Gas-Blood Interface	147
3-7.	Compartment Model to Represent Time-Dependent Particle Transport in the Respiratory	
	Tract	148
3-8.	The Human Respiratory Tract Model: Absorption into Blood	151
3-9.	ICRP (1993) Model of Strontium Biokinetics	153
3-10.	Existing Information on Health Effects of Stable Strontium	180
3-11.	Existing Information on Health Effects of Radioactive Strontium	181
6-1.	Frequency of NPL Sites with Strontium Contamination	212
6-2.	Major DOE Offices, Facilities, and Laboratories	220
6-3.	U.S. Daily Dietary Intake of 90Sr, 1961–1992	242

STRONTIUM xx

LIST OF TABLES

3-1.	Levels of Significant Exposure to Strontium—Radiation Toxicity—Inhalation	40
3-2.	Levels of Significant Exposure to Strontium—Chemical Toxicity—Oral	57
3-3.	Levels of Significant Exposure to Strontium—Radiation Toxicity—Oral	68
3-4.	Levels of Significant Exposure to Strontium—Radiation Toxicity—External	107
3-5.	Genotoxicity of Stable and Radioactive Strontium In Vivo	122
3-6.	Genotoxicity of Stable and Radioactive Strontium In Vitro	123
3-7.	Summary of Estimates of Absorption of Ingested Strontium in Humans	128
3-8.	Reference Respiratory Values for a General Caucasian Population at Different Levels of	
	Activity	144
3-9.	Reference Values of Parameters for the Compartment Model to Represent Time-dependent	
	Particle Transport from the Human Respiratory Tract	145
4- 1.	Chemical Identity of Strontium and Strontium Compounds	196
4-2.	Physical and Chemical Properties of Strontium and Strontium Compounds	199
4-3.	Percent Natural Occurrence and Radioactive Properties of Isotopes of Strontium	202
6-1.	Radiostrontium Releases from Nuclear Power Plants for 1993	215
6-2.	Selected Bioconcentration Factors for 90Sr in Aquatic, Wetland, and Terrestrial Ecosystems	
	at the Savannah River Site	225
6-3.	Average or Ranges of Concentration of Strontium in Earth Materials	228
6-4.	⁹⁰ Sr in Drinking Water (Composites) for January–December 1995	231
6-5.	Quarterly and Annual Deposition of 90Sr in Selected U.S. Cites for the Year 1990	234
6-6.	Concentration of Strontium in Fruit Juices and Produce	236
6-7.	⁹⁰ Sr in the Human Diets During 1982	238
6-8.	⁹⁰ Sr in Pasteurized Milk in July 1997	240
6-9 .	Strontium Concentrations in Human Body Fluids and Tissues	245
6-10.	Ongoing Studies on Environmental Effects of Strontium	251
7-1.	Analytical Methods for Determining Strontium in Biological Samples	254
7-2.	Analytical Methods for Determining Strontium in Environmental Samples	257
8-1.	Regulations and Guidelines Applicable to Stable Strontium	265
8-2.	Regulations and Guidelines Applicable to Radioactive Strontium	267
8-3.	Effective Dose Coefficients (e(50)) and Annual Limits on Intake (ALI) for Occupational	
	Exposures to Radioactive Strontium Isotopes	281